

What is claimed is:

1. Microspheres useful for embolization wherein said microspheres comprise crosslinked polyvinylalcohol and have a diameter ranging from about 10 μm to about 2,000 μm .

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2. The microspheres of claim 1 wherein said microspheres are substantially spherical.

3. The microspheres of claim 1 wherein said microspheres are substantially uniform in size and shape.

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4. The microspheres of claim 1 wherein the diameter of said microspheres is in the range from about 50 μm to about 1,000 μm .

5. The microspheres of claim 1 wherein said microspheres further comprise a cell adhesion promoter.

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6. The microspheres of claim 5 wherein the cell adhesion promoter is selected from the group consisting of CM dextran, collagen, DEAE dextran, gelatin, glucosaminoglycans, fibronectin, lectins, polycations, a natural biological cell adhesion agent and a synthetic biological cell adhesion agent.

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7. The microspheres of claim 6 wherein the cell adhesion promoter is selected from the group consisting of CM dextran, collagen and DEAE dextran.

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8. The microspheres of claim 1 wherein said microspheres further comprise a marking agent.

9. The microspheres of claim 8 wherein the marking agent is selected from the group consisting of a dye, an imaging agent and a contrasting agent.

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10. The microspheres of claim 1, further comprising an anti-angiogenic agent.

11. An injectable suspension suitable for embolization, which comprises crosslinked polyvinylalcohol
5 microspheres, having a diameter ranging from about 10 μm to about 2,000 μm , and a suitable liquid carrier.

12. The injectable suspension of claim 11 wherein the crosslinked polyvinylalcohol microspheres are substantially spherical.

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13. The injectable suspension of claim 11 wherein the crosslinked polyvinylalcohol microspheres are substantially uniform in size and shape.

14. The injectable suspension of claim 11 which
15 injectable suspension is sterile.

15. The injectable suspension of claim 11 wherein the diameter of the crosslinked polyvinylalcohol microspheres are in the range from about 50 μm to about 1,000 μm .

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16. The injectable suspension of claim 11, wherein the crosslinked polyvinylalcohol microspheres in the injectable suspension are comprised of from about 0.5% to about 20% crosslinked polyvinylalcohol by weight in hydrogel form.

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17. The injectable suspension of claim 11 wherein said crosslinked polyvinylalcohol microspheres further comprise a cell adhesion promoter.

18. The injectable suspension of claim 17 wherein the cell adhesion promoter is selected from the group
30 consisting of CM dextran, collagen, DEAE dextran, gelatin, glucosaminoglycans, fibronectin, lectins, polycations, a

natural biological cell adhesion agent and a synthetic biological cell adhesion agent.

19. The injectable suspension of claim 11 wherein said crosslinked polyvinylalcohol microspheres further
5 comprise a marking agent.

20. The injectable suspension of claim 19 wherein the marking agent is selected from the group consisting of a dye, an imaging agent and a contrasting agent.

10 21. The injectable suspension of claim 11, further comprising an anti-angiogenic agent.

22. A method for prophylactic or therapeutic embolization in a mammal which comprises administering to said mammal in need of such embolization, an injectable
15 suspension comprising an effective amount of crosslinked polyvinylalcohol microspheres, having a diameter ranging from about 10 μm to about 2,000 μm , and a suitable liquid carrier.

23. The method of claim 22 wherein the mammal is a human.
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24. The method of claim 22 wherein said crosslinked polyvinylalcohol microspheres in the injectable suspension are substantially uniform in size and shape.

25 25. The method of claim 22, wherein the crosslinked polyvinylalcohol microspheres in the injectable suspension are comprised of from about 0.5% to about 20% crosslinked polyvinylalcohol by weight in hydrogel form.

26. The method of claim 22 wherein said crosslinked polyvinylalcohol microspheres further comprise a
30 cell adhesion promoter.

27. The method of claim 26 wherein the cell adhesion promoter is selected from the group consisting of CM dextran, collagen, DEAE dextran, gelatin, glucosaminoglycans, fibronectin, lectins, polycations, a natural biological cell adhesion agents and a synthetic biological cell adhesion
5 agent.

28. The method of claim 27 wherein the cell adhesion promoter is selected from the group consisting of CM dextran, collagen and DEAE dextran.

10 29. The method of claim 22 wherein said crosslinked polyvinylalcohol microspheres further comprise a marking agent.

30. The method of claim 29 wherein the marking agent is selected from the group consisting of a dye, an
15 imaging agent and a contrasting agent.

31. The method of claim 22, said crosslinked polyvinylalcohol microspheres further comprise an anti-angiogenic agent.

20 32. A process for producing crosslinked polyvinylalcohol microspheres, having a diameter ranging from about 10 μm to about 2,000 μm , which comprises:

- a) dissolving polyvinylalcohol in an acidic solution;
- b) adding an aldehyde to said polyvinylalcohol-containing solution, or vice verse, to form a
25 mixture;
- c) adding said mixture, with agitation, to an oil containing from about 0.1% to about 10% of an emulsifier having HLB less than 5, or vice verse, to form an emulsion with droplets of
30 polyvinylalcohol suspended in said oil;

- d) heating said emulsion to condense said aldehyde on polyvinylalcohol chains and thereby forming spherical particles of crosslinked polyvinylalcohol;
- 5 e) removing said oil from said spherical particles of crosslinked polyvinylalcohol;
- f) neutralizing said active aldehyde on said spherical particles of crosslinked polyvinylalcohol; and
- g) washing said neutralized spherical particles of crosslinked polyvinylalcohol with a physiological aqueous buffer.

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33. The process of claim 32 which further comprises the step of sterilizing said washed spherical particles of crosslinked polyvinylalcohol.

15 34. The process of claim 32, wherein in step (b) the aldehyde is selected from the group consisting of formaldehyde, glyoxal, glutaraldehyde and terephthalaldehyde.

35. The process of claim 34, wherein the aldehyde is glutaraldehyde.

20 36. The process of claim 32, wherein in step (c) the oil is selected from the group consisting of vegetal oil, mineral oil and non-polar solvent.

25 37. The process of claim 36, wherein the oil is paraffin oil.

30 38. The process of claim 32, wherein in step (c) the emulsifier having HLB less than 5 is selected from the group consisting of sorbitan sesquioleate, sorbitan trioleate, sorbitan tristearate, polyethylene sorbitan monostearate, cellulose acetate butyrate and tetradecanol.

39. The process of claim 32, wherein in step (c) the emulsifier is present in a concentration from about 0.05% to about 5%.

40. The process of claim 32, wherein in step (d) the heating is conducted at about 80°C for about 6 hours.

41. The process of claim 32, wherein in step (e) said oil is removed from said spherical particles of crosslinked polyvinylalcohol by extraction with a light non-polar solvent or chlorinated solvent.

42. The process of claim 41, wherein the light non-polar solvent or chlorinated solvent is methylene chloride.

43. The process of claim 32, wherein in step (f) said active aldehyde on said spherical particles of crosslinked polyvinylalcohol is neutralized by an aminoalcohol.

44. The process of claim 43, wherein said aminoalcohol is selected from the group consisting of Tris, 2-aminoethanol, aminosorbitol and glucosamine.

45. The process of claim 32, further comprising adding a cell adhesion promoter to the acidic polyvinylalcohol solution before adding the aldehyde.

46. The process of claim 45, wherein the cell adhesion promoter is selected from the group consisting of CM dextran, collagen, DEAE dextran, gelatin, glucosaminoglycans, fibronectin, lectins, polycations, a natural biological cell adhesion agents and a synthetic biological cell adhesion agent.

47. The process of claim 32, further comprising absorbing a marking agent into the crosslinked polyvinylalcohol-containing microspheres.

5 48. The process of claim 47, wherein the marking agent is selected from the group consisting of a dye, an imaging agent and a contrasting agent.

49. The process of claim 32, further comprising absorbing an anti-angiogenic agent into the crosslinked polyvinylalcohol microspheres.

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50. The microspheres of claim 5 wherein said microspheres further comprise a marking agent.

51. The microspheres of claim 5, further comprising an anti-angiogenic agent.

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52. The microspheres of claim 8, further comprising an anti-angiogenic agent.

53. The injectable suspension of claim 17 wherein said crosslinked polyvinylalcohol microspheres further
20 comprise a marking agent.

54. The method of claim 26 wherein said crosslinked polyvinylalcohol microspheres further comprise a marking agent.

25 55. The process of claim 38 wherein in step (c) the emulsifier is present in a concentration from about 0.05% to about 5%.

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